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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/516,982	06/21/2005	James T. Kadonaga	00015-023US1/SD2002-201-1	1391

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EXAMINER	
STRZELECKA, TERESA E	
ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
12/31/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/516,982	KADONAGA ET AL.	
	Examiner	Art Unit	
	TERESA E. STRZELECKA	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-33* is/are pending in the application.

4a) Of the above claim(s) *4,6,7,9,11,12,14,15,18,20 and 22-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,8,10,13,16,17,19,21 and 30-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 3, 2008 has been entered.

2. Claims 1and 4-33 were previously pending, with claims 4, 6, 7, 9, 11, 12, 14, 15, 18, 20 and 22-29 withdrawn from consideration. Applicants amended claims 1 and 30. Claims 1, 5, 8, 10, 13, 16, 17, 19, 21 and 30-33 will be examined.

3. Applicants' amendments overcame the objection to claims 1, 5, 8, 10, 13, 16, 17, 19, 21, 31 and 32; the rejection of claims 1, 10, 13, 16, 17, 19, 21 and 30-33 under 35 U.S.C. 102(b) as being anticipated by Wiesmuller et al. Applicants' indication of a support for the limitation "recombinant recombinase" obviated the rejection of claim 5 under 35 U.S.C. 112, first paragraph. All other previously presented rejections are maintained for reasons given in the "Response to Arguments" below.

4. This office action contains new grounds for rejection.

Response to Arguments

5. Applicant's arguments filed September 6, 2008 have been fully considered but they are not persuasive.

Regarding the rejection of claims 1, 5, 8, 10, 13, 16, 17 and 30-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Datta et al., Applicants argue that association of SV40 with histones requires a cell and that they do not teach or suggest forming an "exogenous" nucleosomal polynucleotide and delivery of such polynucleotide to a cell.

However, Datta et al. teach forming nucleosomal polynucleotides in vitro, since they teach reaction of the SV40 plasmid DNA with HeLa cell-free extracts, which contains all of the proteins originally present in the cell (see page 18019, paragraphs 8 and 9). Further, the claims do not require delivery of the nucleosomal polypeptide to a cell: all that is required by the claims is contacting the nucleosomal polynucleotide with a target nucleic acid.

The rejection is maintained.

Claim Interpretation

6. Applicants described the term "nucleosomal polynucleotide" on page 8, paragraph [0025], as follows:

"As used herein, a "nucleosomal polynucleotide" includes any nucleic acid associated with histone core proteins, or histone-like core proteins, forming a chromatin-like structure." Therefore, it is interpreted as any nucleic acid associated with histones or other proteins, as Applicants did not define the terms "histone-like core-proteins" or "chromatin-like structure".

7. Applicants defined the term "exogenous nucleosomal polynucleotide" on page 10, [0030], as follows:

"As used herein, an "exogenous nucleosomal polynucleotide" is a polynucleotide which is transferred into a target cell but which has not been replicated in that host cell;"

8. Applicants defined the term "target nucleic acid sequence" on page 10, [0032], as follows:

"As used herein, the term "target nucleic acid sequence" refers to polynucleotide sequences suitable for recombination with a nucleosomal polynucleotide." Therefore the term is interpreted as any nucleic acid sequence.

9. Applicants defined the term "recombinase" on page 11, [0033], as follows:

"As used herein, "recombinase" refers to polypeptides having essentially all or most of the same functions, particularly the recombinase can: (i) properly bind to and position a nucleosomal polynucleotide to a homologous target and (ii) facilitate homologous recombination."

10. Applicants did not define the term "isolated recombinase", therefore any recombinase that is not contained within live cells is considered to anticipate this term.

11. Applicants did not define the term "Rad51 associated activity", therefore it is interpreted as any recombinase activity.

12. Applicants did not define the term "plasmid", therefore it is interpreted as any nucleic acid vector or virus.

Claim Rejections - 35 USC § 112

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 1, 5, 8, 10, 13, 16, 17, 19, 21 and 30-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1, 5, 8, 10, 13, 16, 17, 19, 21, 31 and 32 are indefinite in claim 1. Claim 1 is indefinite over the recitation of "recombinase comprising Rad51 associated activity". It is not clear what is encompassed by this term. For example, does a protein containing a fragment of Rad51 protein have "Rad51 associated activity"? Or is it any recombinase?

B) Claims 30 and 33 are indefinite in claim 30. Claim 30 is indefinite over the recitation of "recombinase comprising Rad51 associated activity". It is not clear what is encompassed by this term. For example, does a protein containing a fragment of Rad51 protein have "Rad51 associated activity"? Or is it any recombinase?

C) Claim 32 is indefinite over the recitation of "wherein the proteins that promote chromatin formation are selected from the group consisting of ACF, NAP1, topoisomerase I, histones and any combinations thereof". Claim 32 depends from claim 1, which, in the first step of the method, requires contacting a polynucleotide with proteins that promote chromatin formation to generate a polynucleotide comprising histones. Therefore, it seems that contacting the polynucleotides with at least histones is required, otherwise the polynucleotide produced would not contain them. Therefore, it is not clear how contacting the polynucleotide with the ACF protein, for example, would produce polynucleotides containing histones.

D) Claim 33 is indefinite over the recitation of "wherein the proteins that promote chromatin formation are selected from the group consisting of ACF, NAP1, topoisomerase I, histones and any combinations thereof". Claim 33 depends from claim 30, which, in the first step of the method, requires contacting a polynucleotide with proteins that promote chromatin formation to generate a polynucleotide comprising core histones. Therefore, it seems that contacting the polynucleotides with at least core histones is required, otherwise the polynucleotide produced would not contain them. Therefore, it is not clear how contacting the polynucleotide with the ACF protein, for example, would produce polynucleotides containing core histones.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 1, 5, 8, 10, 13, 16, 17, 19, 21 and 30-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Datta et al. (J. Biol. Chem., vol. 276, pp. 18018-18023, May 2001; cited in the

previous office action) as evidenced by Polisky et al. (PNAS USA, vol. 72, pp. 2895-2899, 1975; cited in the previous office action).

Claims 1 and 30 will be considered together in claim 1, since it is a species of claim 30.

Regarding claims 1 and 30, Datta et al. teach a method of promoting homologous recombination, the method comprising:

Generating an exogeneous nucleosomal polynucleotide in vitro comprising (Abstract):

contacting an isolated relaxed polynucleotide comprising a desired sequence to be recombined with proteins that promote chromatin formation to generate a nucleosomal polynucleotide comprising histones; contacting, under conditions that support homologous recombination, the exogenous polynucleotide with a target nucleic acid, wherein the target nucleic acid comprises a nucleotide sequence homologous to the nucleosomal polynucleotide; and contacting the nucleosomal polynucleotide and target nucleic acid with a recombinase comprising Rad51 associated activity (Datta et al. teach providing an SV40-based plasmid pSupFG1/G144C (= isolated polynucleotide) with a 40 bp fragment homologous to bp 121-160 of the supFG1-144 gene (page 18019, second and third paragraph; Fig. 1) and a donor oligonucleotide (= target nucleic acid) (page 18019, second and fourth paragraph; Fig. 1) under conditions which promote homologous recombination (page 18019, paragraphs 8 and 9; page 18020, second and third paragraph), where recombination in HeLa cell-free extracts is taught. As evidenced by Polisky et al. SV40 particles associate with histones (page 2895, paragraphs 2-4), therefore, by teaching SV40 plasmid in eukaryotic cell extract, Datta et al. inherently teach nucleosomal polynucleotides. Datta et al. teach Rad51 associated recombinase activity (page 18019, second paragraph; page 18020, 6th paragraph).).

Regarding claim 5, Datta et al. teach recombinase in a cell extract (page 18019, paragraphs 8 and 9), therefore they teach isolated recombinase.

Regarding claim 8, Datta et al. teach recombination in a cell extract in vitro (page 18019, paragraphs 8 and 9).

Regarding claim 10, Datta et al. teach exogenous target sequence (page 18019, fourth paragraph; Fig. 1).

Regarding claim 13, Datta et al. teach a sequence coding for a supFG1-144 gene (Fig. 1).

Regarding claims 16, 32 and 33, Datta et al. teach SV40-based plasmid within eukaryotic cell extract (page 18019, 9th paragraph). As evidenced also by Polisky et al. SV40 particles associate with histones in monkey cells (page 2895, paragraphs 2-4) and core histones (Abstract; page 2896, paragraphs 4-6). Therefore, by teaching SV40 plasmid within eukaryotic cells Datta et al. teach nucleosomal polynucleotide associated with core histones.

Regarding claim 17, Datta et al. teach SV40-based plasmid (Fig. 1).

Regarding claims 19, 21 and 31, Datta et al. teach that the polynucleotide contains a genetic mutation which alters the expression of tRNA gene (page 18019, last two paragraphs; page 18020, paragraphs 1-3; Fig. 1 and 2).

17. No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TERESA E. STRZELECKA whose telephone number is (571)272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Teresa E Strzelecka
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December 22, 2008